CERTIFICATE OF MAILING
37 C.F.R. § 1.8

I hereby certify that this correspondence is being deposited with the U.S. Postal Service with sufficient postage as First Class Mail in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on the date below:

October 9, 2006
Date

Shelley P.M. Fussey

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:
Philip E. Thorpe and Sophia Ran (As Amended)

Serial No.: 10/621,269

Filed: July 15, 2003

For: Selected Antibody Compositions for Binding to Aminophospholipids (As Amended)

Group Art Unit: 1642

Examiner: Goddard, L.

Atty. Dkt. No.: 4001.003000

DECLARATION OF
PHILIP E. THORPE UNDER 37 C.F.R. §1.132

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

I, PHILIP E. THORPE, HEREBY DECLARE AS FOLLOWS:

1. I am a co-inventor of the subject matter disclosed and claimed in the captioned patent application.

2. I am Professor of Pharmacology and hold the Serena S. Simmons Distinguished Chair in Immunopharmacology at the Simmons Cancer Center, The University of Texas Southwestern Medical Center at Dallas, Dallas, Texas, U.S.A. A copy of my *Curriculum Vitae* is attached as **Exhibit A**.

3. I have reviewed the captioned patent application again. I understand the claims in the captioned patent application to be drawn to purified antibodies, or antigen-binding fragments thereof, that bind to phosphatidylserine (PS) and effectively compete with the monoclonal antibody 3G4 for binding to PS; and to compositions comprising, hybridomas producing and methods for preparing such antibodies.

4. I have reviewed the Official Action issued by the U.S. Patent and Trademark Office (P.T.O.), the agency charged with assessing the patentability of the captioned patent application.

5. I understand that the P.T.O. has taken the position that claims drawn to pharmaceutical compositions of such antibodies are not adequately supported by the specification portion of the captioned patent application, *i.e.*, that the specification does not provide enough guidance for a trained scientist to reasonably be able to prepare and use such pharmaceutical compositions.

6. I disagree with the assessment that the specification does not provide sufficient teaching to enable a skilled scientist to prepare and use the claimed pharmaceutical compositions. I understand that a response will be filed explaining various reasons why the specification does provide the required teaching.

7. I further understand that one of the main reasons underlying the P.T.O.'s questioning of the pharmaceutical composition claims is that it is not clear from the specification that the 3G4 and 9D2 antibodies effectively compete with each other for binding to PS. I disagree that such a

showing would be required for a skilled scientist to reasonably be able to prepare and use the claimed pharmaceutical compositions.

8. Nonetheless, I am providing the present Declaration and providing the attached evidence to demonstrate that the 3G4 antibody effectively competes with the 9D2 antibody for binding to PS. This evidence satisfies the P.T.O.'s request for additional data to show that the pharmaceutical composition claims are adequately supported by the specification of the captioned patent application.

9. Evidence of the fact that 3G4 effectively competes with 9D2 for binding to PS is presented in **Exhibit B**, which shows the results of a competition study using the 3G4 and 9D2 antibodies.

10. The data of **Exhibit B** were generated from a competitive binding ELISA. The ELISA itself is conducted in accordance with Example IV of the specification. Briefly, PS was dissolved in hexane and dried on a 96-well ELISA plate. The plate was blocked using 1% BSA for 1 hour. All antibodies were diluted in 1% BSA. The competitive assay was conducted using a 50 μM starting concentration of 9D2, and excesses of 3G4 (or ch3G4) were added up to a 200:1 molar ratio of 3G4 (or ch3G4) to 9D2. The plates were then washed, and bound 9D2 antibody was detected using an anti-rat secondary antibody conjugated to horseradish peroxidase, followed by a development step.

11. In the competitive binding ELISA, as 9D2 is a rat antibody (specification, Example IV, Table 2), 9D2 binding to the PS-coated plate is detected using an anti-rat secondary antibody.

Any 3G4 that binds to the PS-coated plate is not detected in this assay, as 3G4 is a mouse antibody. In addition to the original murine 3G4 antibody, the competitive binding ELISA also tested competition using a chimeric form of 3G4 (ch3G4), in which the mouse variable regions of the 3G4 antibody are linked to human IgG constant regions. Chimeric 3G4 binds to PS in the same manner as murine 3G4, by virtue of the mouse variable regions. Again, any ch3G4 that binds to the PS-coated plate is not detected in this assay, as the anti-rat secondary antibody does not detect human constant regions.

12. **Exhibit B** shows the results of the competitive binding ELISA, which are plotted as percentage inhibition of 9D2 binding *vs.* fold excess of 3G4 or ch3G4. As shown in **Exhibit B**, increasing the amount of 3G4 (♦) or chimeric 3G4 (■) progressively inhibits 9D2 binding to PS. The data in **Exhibit B** therefore show that the 3G4 antibody effectively competes with the 9D2 antibody for binding to PS.

13. I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the captioned patent application or any patent issued thereon.

October 3, 2006
Date

Philip E. Thorpe

Philip E. Thorpe, Ph.D.